

WHAT IS CLAIMED IS:

1. A method for protection of a tissue or an organ from damage by a cytotoxic agent comprising administering an effective amount of a TGF- $\alpha$  polypeptide (SEQ ID NO:1), a TGF- $\alpha$  related polypeptide, a TGF- $\alpha$ 57 polypeptide (SEQ ID NO:3), a functional fragment thereof or a mimetic thereof to the tissue or organ prior to, simultaneously with or subsequent to contacting the tissue or organ with the cytotoxic agent.
2. The method of claim 1, wherein the organ or tissue is selected from the group consisting gastrointestinal tissue, urogenital tissue, musculoskeletal tissue, nerve tissue, or cardiovascular tissue.
3. A method for treating, regenerating or repairing a tissue of a subject *in vivo*, comprising:  
contacting a tissue with a TGF-  $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a fragment or a mimetic thereof prior to, contemporaneously with, or subsequent to a tissue injury in an amount effective to induce stem cell or precursor cell proliferation, migration, or differentiation at the site of injury thereby treating, regenerating or repairing the tissue.
4. The method of claim 3, wherein the contacting is by continuous infusion of the TGF-  $\alpha$  polypeptide, fragment or mimetic.
5. The method of claim 3, wherein the contacting is by a bolus or single administration of the TGF-  $\alpha$  polypeptide, fragment or mimetic.
6. The method of claim 4, wherein the tissue is a musculoskeletal tissue, a gastrointestinal tissue, or a urogenital tissue.
7. The method of claim 5, wherein the tissue is selected from the group consisting of a musculoskeletal tissue, a gastrointestinal tissue, a urogenital tissue, and a neurological tissue.

8. The method of claim 3, wherein the stem cell is an adult stem cell.
9. The method of claim 3, wherein the stem cell is a tissue specific precursor cell.
10. The method of claim 3, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:1.
11. The method of claim 3, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:3.
12. The method of claim 3, wherein the polypeptide has a sequence NH<sub>2</sub>- X<sub>1a</sub> - Cys - His - Ser - X<sub>1b</sub> - X<sub>2</sub> - X<sub>1a</sub> - X<sub>1b</sub> - X<sub>1a</sub> - X<sub>3</sub> - Cys COOH (SEQ ID NO:4) wherein X<sub>1a</sub> and X<sub>1b</sub> are independently Val, Gly or Ala; X<sub>2</sub> is Tyr or Phe; X<sub>3</sub> is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional peptide having TGF- $\alpha$  activity.
13. The method of claim 12, wherein at least one or more of the following amino acids are linked to the C-terminal Cys moiety of SEQ ID NO:4: - X<sub>4</sub> - His - X<sub>1c</sub> - X<sub>4</sub> - X<sub>5</sub> - X<sub>6</sub> - X<sub>1c</sub> (SEQ ID NO:5) wherein X<sub>4</sub> is Glu or Asp; X<sub>5</sub> is Leu or Ile; and X<sub>6</sub> is Asp or Glu.
14. The method of claim 13, wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly and X<sub>1c</sub> is Ala.
15. The method of claim 13, wherein X<sub>2</sub> is Tyr and X<sub>3</sub> is Arg.
16. The method of claim 13, wherein the functional peptide is 18 amino acids in length wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly, X<sub>1c</sub> is Ala and X<sub>4</sub> is Gly.
17. The method of claim 3, wherein the TGF- $\alpha$  related polypeptide is selected from the group consisting of vaccinia growth factor, amphiregulin precursor, betacellulin precursor, heparin binding EGF-like growth factor, epiregulin,

HUS 19878, myxomavirus growth factor (MGF), Shope fibroma virus growth factor (SFGF), and schwannoma derived growth factor.

18. The method of claim 3, wherein the tissue injury results from cytotoxic or immune-suppressing therapy.
19. The method of claim 3, wherein the injury results from ARC or AIDS.
20. The method of claim 3, wherein the subject is a mammal.
21. The method of claim 20, wherein the mammal is a human.
22. The method of claim 3, wherein the contacting is at the site of tissue injury.
23. A method for treating, inhibiting or preventing mucositis of the gastrointestinal tract in a subject comprising administering a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a TGF- $\alpha$ 57 polypeptide, a fragment thereof, or a mimetic thereof in an amount effective to treat, inhibit or prevent gastrointestinal mucositis in the subject.
24. The method of claim 23, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:1.
25. The method of claim 23, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:3.
26. The method of claim 23, wherein the polypeptide has a sequence NH<sub>2</sub>- X<sub>1a</sub> - Cys - His - Ser - X<sub>1b</sub> - X<sub>2</sub> - X<sub>1a</sub> - X<sub>1b</sub> - X<sub>1a</sub> - X<sub>3</sub> - Cys COOH (SEQ ID NO:4) wherein X<sub>1a</sub> and X<sub>1b</sub> are independently Val, Gly or Ala; X<sub>2</sub> is Tyr or Phe; X<sub>3</sub> is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional peptide having TGF- $\alpha$  activity.

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27. The method of claim 26, wherein at least one or more of the following amino acids are linked to the C-terminal Cys moiety of SEQ ID NO:4: - X<sub>4</sub> - His - X<sub>1c</sub> - X<sub>4</sub> - X<sub>5</sub> - X<sub>6</sub> - X<sub>1c</sub> (SEQ ID NO:5) wherein X<sub>4</sub> is Glu or Asp; X<sub>5</sub> is Leu or Ile; and X<sub>6</sub> is Asp or Glu.
  28. The method of claim 27, wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly and X<sub>1c</sub> is Ala.
  29. The method of claim 27, wherein X<sub>2</sub> is Tyr and X<sub>3</sub> is Arg.
  30. The method of claim 27, wherein the functional peptide is 18 amino acids in length wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly, X<sub>1c</sub> is Ala and X<sub>4</sub> is Gly.
  31. The method of claim 23, wherein the TGF- $\alpha$  related polypeptide is selected from the group consisting of vaccinia growth factor, amphiregulin precursor, betacellulin precursor, heparin binding EGF-like growth factor, epiregulin, HUS 19878, myxomavirus growth factor (MGF), Shope fibroma virus growth factor (SFGF), and schwannoma derived growth factor.
  32. The method of claim 23, wherein the gastrointestinal mucositis results from cytotoxic or immune-suppressing therapy.
  33. The method of claim 23, wherein the mucositis results from ARC or AIDS.
  34. The method of claim 23, wherein the subject is a mammal.
  35. The method of claim 34, wherein the mammal is a human.
  36. A method for expansion of a precursor cell comprising contacting the cell *in vitro* with an amount of a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to promote precursor cell proliferation, and culturing the cell *in vitro* under growth conditions such that the cell proliferates.

37. The method of claim 36, wherein the precursor cell is of ectodermal origin.
38. The method of claim 36, wherein the precursor cell is of endodermal origin.
39. The method of claim 36, wherein the precursor cell is of mesodermal origin.
40. The method of claim 36, wherein the precursor cell is selected from the group consisting of hematopoietic precursor cells, epithelial precursor cells, kidney precursor cells, neural precursor cells, skin precursor cells, osteoblast precursor cells, chondrocyte precursor cells, and liver precursor cells.
41. The method of claim 36, wherein the TGF- $\alpha$  polypeptide has a sequence as set forth in SEQ ID NO:1.
42. The method of claim 36, wherein the TGF- $\alpha$  polypeptide has a sequence NH<sub>2</sub>-X<sub>1a</sub> - Cys - His - Ser - X<sub>1b</sub> - X<sub>2</sub> - X<sub>1a</sub> - X<sub>1b</sub> - X<sub>1a</sub> - X<sub>3</sub> - Cys - COOH (SEQ ID NO:4) wherein X<sub>1a</sub> and X<sub>1b</sub> are independently Val, Gly or Ala; X<sub>2</sub> is Tyr or Phe; X<sub>3</sub> is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional fragment having TGF- $\alpha$  activity.
43. The method of claim 42, wherein at least one or more of the following amino acids are linked to the C-terminal Cys moiety of SEQ ID NO:4:  
- X<sub>4</sub> - His - X<sub>1c</sub> - X<sub>4</sub> - X<sub>5</sub> - X<sub>6</sub> - X<sub>1c</sub> (SEQ ID NO:5) wherein X<sub>4</sub> is Glu or Asp; X<sub>5</sub> is Leu or Ile; and X<sub>6</sub> is Asp or Glu.
44. The method of claim 43, wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly and X<sub>1c</sub> is Ala.
45. The method of claim 43, wherein X<sub>2</sub> is Tyr and X<sub>3</sub> is Arg.

46. The method of claim 43, wherein the functional fragment is 18 amino acids in length and X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly, X<sub>1c</sub> is Ala and X<sub>4</sub> is Gly.
47. The method of claim 36, wherein the TGF- $\alpha$  polypeptide has a sequence as set forth in SEQ ID NO:3.
48. The method of claim 36, wherein the TGF- $\alpha$  related polypeptide is selected from the group consisting of vaccinia growth factor, amphiregulin precursor, betacellulin precursor, heparin binding EGF-like growth factor, epiregulin, HUS 19878, myxomavirus growth factor (MGF), Shope fibroma virus growth factor (SFGF), and schwannoma derived growth factor.
49. The method of claim 36, wherein the precursor cell is a hematopoietic stem cell.
50. The method of claim 36, wherein the precursor cell contains a recombinant nucleic acid encoding a protein of value in the treatment of a human disease or disorder.
51. The method of claim 36, wherein the contacting is carried out by a method comprising exposing the precursor cell to cells recombinantly expressing the TGF- $\alpha$  polypeptide, functional fragment thereof, or a mimetic thereof.
52. The method of claim 36, wherein the contacting is carried out by culturing the precursor cell in medium containing a substantially pure TGF- $\alpha$  polypeptide, functional fragment thereof, or a mimetic thereof.
53. The method of claim 36, wherein substantially no differentiation of the precursor cell occurs.
54. The method of claim 36, wherein the precursor cells are in a mixed population of cells.

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55. The method of claim 36, wherein the precursor cells are substantially enriched.
  56. A method for expansion of a precursor cell population comprising recombinantly expressing within the cell an amount of a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to induce proliferation of the cells; and culturing the cells under conditions such that the cell proliferates, thereby expanding the cell population.
  57. A method for expansion of a hematopoietic precursor cell population comprising recombinantly expressing within the cell an amount of a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to induce proliferation of the cells; and culturing the cells under conditions such that the cell proliferates, thereby expanding the cell population.
  58. A method for expansion of an epithelial precursor cell population comprising recombinantly expressing within the cell an amount of a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to induce proliferation of the cells; and culturing the cells under conditions such that the cell proliferates, thereby expanding the cell population.
  59. A method for expansion of a liver precursor cell population comprising recombinantly expressing within the cell an amount of a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to induce proliferation of the cells; and culturing the cells under conditions such that the cell proliferates, thereby expanding the cell population.

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60. A method for expansion of a human precursor cell population comprising contacting the precursor cell *in vitro* with a second cell wherein the second cell recombinantly expresses a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to induce proliferation of the cells; and culturing the cells under conditions such that the cell proliferates, thereby expanding the cell population.
  61. A method for inducing proliferation of mammalian neuronal cells comprising contacting a mammalian neuron *in vitro* with a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof effective to induce proliferation of the cells; and culturing the cells under conditions such that the cell proliferates.
  62. A method for expanding stem cells *ex vivo*, comprising:
    - (a) culturing stem cells from a subject;
    - (b) contacting the stem cell culture with a TGF- $\alpha$  polypeptide, a TGF- $\alpha$  related polypeptide, a functional fragment thereof, or a mimetic thereof in an amount necessary to expand the stem cells.
  63. The method of claim 62, wherein the TGF- $\alpha$  polypeptide has a sequence as set forth in SEQ ID NO:1.
  64. The method of claim 62, wherein the TGF- $\alpha$  polypeptide has a sequence NH<sub>2</sub>-X<sub>1a</sub> - Cys - His - Ser - X<sub>1b</sub> - X<sub>2</sub> - X<sub>1a</sub> - X<sub>1b</sub> - X<sub>1a</sub> - X<sub>3</sub> - Cys - COOH (SEQ ID NO:4) wherein X<sub>1a</sub> and X<sub>1b</sub> are independently Val, Gly or Ala; X<sub>2</sub> is Tyr or Phe; X<sub>3</sub> is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional fragment having TGF- $\alpha$  activity.
  65. The method of claim 64, wherein at least one or more of the following amino acids are linked to the C-terminal Cys moiety of SEQ ID NO:4:

- X<sub>4</sub> - His - X<sub>1c</sub> - X<sub>4</sub> - X<sub>5</sub> - X<sub>6</sub> - X<sub>1c</sub> (SEQ ID NO:5) wherein X<sub>4</sub> is Glu or Asp; X<sub>5</sub> is Leu or Ile; and X<sub>6</sub> is Asp or Glu.
66. The method of claim 64, wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly and X<sub>1c</sub> is Ala.
67. The method of claim 65, wherein X<sub>2</sub> is Tyr and X<sub>3</sub> is Arg.
68. The method of claim 65, wherein the functional fragment is 18 amino acids in length and X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly, X<sub>1c</sub> is Ala and X<sub>4</sub> is Gly.
69. The method of claim 62, wherein the TGF- $\alpha$  polypeptide has a sequence as set forth in SEQ ID NO:3.
70. The method of claim 62, wherein the TGF- $\alpha$  related polypeptide is selected from the group consisting of vaccinia growth factor, amphiregulin precursor, betacellulin precursor, heparin binding EGF-like growth factor, epiregulin, HUS 19878, myxomavirus growth factor (MGF), Shope fibroma virus growth factor (SFGF), and schwannoma derived growth factor.
71. A method for treating Type I or Type II diabetes by expanding a subject's population of insulin-producing cells, comprising administering an effective amount of a TGF- $\alpha$  polypeptide (SEQ ID NO:1), a TGF- $\alpha$  related polypeptide, a TGF- $\alpha$ 57 polypeptide (SEQ ID NO:3), a fragment thereof, or a mimetic thereof.
72. A method for treating AIDS and HIV infection by increasing a subject's population of CD4+ T cells, comprising administering an effective amount of a TGF- $\alpha$  polypeptide (SEQ ID NO:1), a TGF- $\alpha$  related polypeptide, a TGF- $\alpha$ 57 polypeptide (SEQ ID NO:3), a fragment thereof, or a mimetic thereof.